

FISYDGSNKHYADSVKG (SEQ ID NO:33) and TGWLGPFDY (SEQ ID NO: 37), respectively, and light chain CDR1, CDR2, and CDR3 sequences, RASQSVSSSFLA (SEQ ID NO:25), GASSRAT (SEQ ID NO:30), and QQYGSSPWT (SEQ ID NO:35), respectively.

Please replace the paragraph beginning on page 7, line 13, with the following amended paragraph:

Other human sequence antibodies of the invention comprise heavy chain CDR1, CDR2, and CDR3 sequences, SYGMH (SEQ ID NO:28), VIWYDGSNKYYADSVKG (SEQ ID NO:34) and APNYIGAFDV (SEQ ID NO:38), respectively, and light chain CDR1, CDR2, and CDR3 sequences, RASQGISSWLA (SEQ ID NO:26), AASSLQS (SEQ ID NO:31), and QQYNSYPPT (SEQ ID NO:36), respectively.

Please replace the paragraph beginning on page 8, line 3, with the following amended paragraph:

The invention provides a hybridoma cell line comprising a B cell obtained from a transgenic non-human animal having a genome comprising a human sequence heavy chain transgene and a human sequence light chain transgene, wherein the hybridoma produces a human sequence antibody that specifically binds to human CTLA-4. In a related embodiment, the hybridoma secretes a human sequence antibody that specifically binds human CTLA-4 or binding fragment thereof, wherein the antibody is selected from the group consisting of: a human sequence antibody comprising heavy chain CDR1, CDR2, and CDR3 sequences, SYTMH (SEQ ID NO:27), FISYDGNNKYYADSVKG (SEQ ID NO:32) and TGWLGPFDY (SEQ ID NO:37), respectively, and light chain CDR1, CDR2, and CDR3 sequences, RASQSVGSSYLA (SEQ ID NO:24), GAFSRAT (SEQ ID NO:29), and QQYGSSPWT (SEQ ID NO:35), respectively, and heavy chain and light chain variable region amino acid sequences as set forth in SEQ ID NO:17 and SEQ ID NO:7, respectively; a human sequence antibody comprising heavy chain CDR1, CDR2, and CDR3 sequences, SYTMH (SEQ ID NO:27), FISYDGSNKHYADSVKG

(SEQ ID NO:33) and TGWLGPFDY (SEQ ID NO: 37), respectively, and light chain CDR1, CDR2, and CDR3 sequences, RASQSVSSSFLA (SEQ ID NO:25), GASSRAT (SEQ ID NO:30), and QQYGSSPWT (SEQ ID NO:35), respectively, and heavy chain and light chain variable region amino acid sequences as set forth in SEQ ID NO:19 and SEQ ID NO:9, respectively; or a human sequence antibody of claim 1, comprising heavy chain CDR1, CDR2, and CDR3 sequences, SYGMH (SEQ ID NO:28), VIWYDGSNKYYADSVKG (SEQ ID NO:34) and APNYIGAFDV (SEQ ID NO:38), respectively, and light chain CDR1, CDR2, and CDR3 sequences, RASQGISSWLA (SEQ ID NO:26), AASSLQS (SEQ ID NO:31), and QQYNSYPPT (SEQ ID NO:36), respectively, and heavy chain and light chain variable region amino acid sequences as set forth in SEQ ID NO:23 and SEQ ID NO:13, respectively.

Please replace ⁷⁴ Table 3, on page ~~72~~, lines 1-4, with the following amended table:

Chain	HuMAb	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
Light Chain	10D1 4B6 1E2	RASQSVGSSYLA RASQSVSSSFLA RASQGISSWLA	24 25 26	GAFSRAT GASSRAT AASSLQS	29 30 31	QQYGSSPWT QQYGSSPWT QQYNSYPPT	35 35 36
Heavy Chain	10D1 4B6 1E2	SYTMH SYTMH SYGMH	27 27 28	FISYDGNNKYYADSVKG FISYDGNSNKHYADSVKG VIWYDGSNKYYADSVKG	32 33 34	TGWLGPFDY TGWLGPFDY APNYIGAFDV	37 37 38

Please replace the paragraph beginning on page 76, line 16, with the following amended paragraph:

The kappa light chain plasmid, pCK7-96 (SEQ ID NO:39), includes the kappa constant region and polyadenylation site, such that kappa sequences amplified with 5' primers that include HindIII sites upstream of the initiator methionine can be digested with HindIII and BbsI, and cloned into pCK7-96 digested with HindIII and BbsI to reconstruct a complete light chain coding sequence together with a polyadenylation site. This cassette can be isolated as a HindIII/NotI fragment

b7c
and ligated to transcription promoter sequences to create a functional minigene for transfection into cells.

Please replace the paragraph beginning on page 76, line 23, with the following amended paragraph:

b7c
The gamma1 heavy chain plasmid, pCG7-96 (SEQ ID NO:40), includes the human gamma1 constant region and polyadenylation site, such that gamma sequences amplified with 5' primers that include HindIII sites upstream of the initiator methionine can be digested with HindIII and AgeI, and cloned into pCG7-96 digested with HindIII and AgeI to reconstruct a complete gamma1 heavy chain coding sequence together with a polyadenylation site. This cassette can be isolated as a HindIII/SalI fragment and ligated to transcription promoter sequences to create a functional minigene for transfection into cells.

Please replace the paragraph beginning on page 76, line 31, with the following amended paragraph:

b7c
The gamma4 heavy chain plasmid, pG4HE (SEQ ID NO:41), includes the human gamma4 constant region and polyadenylation site, such that gamma sequences amplified with 5' primers that include HindIII sites upstream of the initiator methionine can be digested with HindIII and AgeI, and cloned into pG4HE digested with HindIII and AgeI to reconstruct a complete gamma4 heavy chain coding sequence together with a polyadenylation site. This cassette can be isolated as a HindIII/EcoRI fragment and ligated to transcription promoter sequences to create a functional minigene for transfection into cells.

Please insert the following paragraph immediately before the paragraph beginning at page 93, line 1 of the specification:

SEQ ID NO:1 pGP1k

b7c
AATTAGCGGC CGCTGTCGAC AAGCTTCGAA TTCACTATCG ATGTGGGGTA 50
CCTACTGTCC CGGGATTGCG GATCCCGCAT GATATCGTTG ATCCTCGAGT 100
GCGGCCGAG TATGCAAAAA AAAGCCCGCT CATTAGGCCGG GCTCTTGGCA 150
GAACATATCC ATCGCGTCCG CCATCTCCAG CAGCCGCACG CGCGCATCT 200
CGGGCAGCGT TGGGTCTGG CCACGGGTGC GCATGATCGT GCTCCTGTCG 250

TTGAGGACCC GGCTAGGCTG GCGGGGTGC CTTACTGGTT AGCAGAAATGA 300
ATCACCGATA CGCGAGCGAA CGTGAAGCGA CTGCTGTCG AAAACGTCTG 350
CGACCTGAGC AACAAACATGA ATGGTCTTCG GTTCCGTGT TTCTGAAAGT 400
CTGGAAACGC GGAAGTCAGC GCCCTGCACC ATTATGTTCC GGATCTGCAT 450
CGCAGGATGC TGCTGGCTAC CCTGTGGAAC ACCTACATCT GTATTAACGA 500
AGCGCTGGCA TTGACCCCTGA GTGATTTTC TCTGGTCCCCG CCGCATCCAT 550
ACCGCCAGTT GTTACCCCTC ACAACGTTCC AGTAACCGGG CATGTTCATC 600
ATCAGTAACC CGTATCGTGA GCATCCTCTC TCGTTTCATC GGTATCATT 650
CCCCCATGAA CAGAAATTCC CCCTTACACG GAGGCATCAA GTGACCAAAC 700
AGGAAAAAAC CGCCCTAAC ATGGCCCGCT TTATCAGAAG CCAGACATTA 750
ACGCTTCTGG AGAAACTCAA CGAGCTGGAC GCGGATGAAC AGGCAGACAT 800
CTGTGAATCG CTTCACGACC ACGCTGATGA GCTTACCGC AGCTGCCTCG 850
CGCGTTTCGG TGATGACGGT GAAAACCTCT GACACATGCA GCTCCCGGAG 900
ACGGTCACAG CTTGTCTGTA AGCGGATGCC GGGAGCAGAC AAGCCCGTCA 950
GGGCGCGTCA CGGGGTGTTG CGGGGTGTCG GGGCGCAGCC ATGACCCAGT 1000
CACGTAGCGA TAGCGGAGTG TATACTGGCT TAACTATGCG GCATCAGAGC 1050
AGATTGTACT GAGAGTGCAC CATATGCGGT GTGAAATACC GCACAGATGC 1100
GTAAGGAGAA AATACCGCAT CAGGCCTCT TCCGCTTCCT CGCTCACTGA 1150
CTCGCTGCCG TCGGTCGTTC GGCTGCGCG AGCGGTATCA GCTCACTCAA 1200
AGGCGGTAAT ACGTTATCC ACAGAATCAG GGGATAACGC AGGAAAGAAC 1250
ATGTGAGCAA AAGGCCAGCA AAAGGCCAGG AACCGTAAAA AGGCCCGT 1300
GCTGGCGTTT TTCCATAGGC TCCGCCCCCC TGACGAGCAT CACAAAAATC 1350
GACGCTCAAG TCAGAGGTGG CGAAACCGA CAGGACTATA AAGATACCAAG 1400
GCGTTCCCC CTGGAAGCTC CCTCGTGC CGTCTCGTTC CGACCCCTGCC 1450
GCTTACCGGA TACCTGTCCG CCTTCTCCC TTCGGGAAGC GTGGCGCTTT 1500
CTCATAGCTC ACGCTGTAGG TATCTCAGTT CGGTGTAGGT CGTTCGCTCC 1550
AAGCTGGCT GTGTGCACGA ACCCCCCGTT CAGCCCCGACC GCTGCGCCTT 1600
ATCCGGTAAC TATCGTCTTG AGTCCAACCC GGTAAAGACAC GACTTATCGC 1650
CACTGGCAGC AGCCAGGCGC GCCTTGGCCT AAGAGGCCAC TGGTAACAGG 1700
ATTAGCAGAG CGAGGTATGT AGGCGGTGCT ACAGAGTTCT TGAAGTGGTG 1750
GCCTAACTAC GGCTACACTA GAAGGACAGT ATTTGGTATC TGCGCTCTGC 1800
TGAAGCCAGT TACCTTCGGA AAAAGAGTTG GTAGCTCTTG ATCCGGCAA 1850
CAAACCACCG CTGGTAGCGG TGGTTTTTT GTTGTCAAGC AGCAGATTAC 1900
GCGCAGAAAA AAAGGATCTC AAGAAGATCC TTTGATCTT TCTACGGGGT 1950
CTGACGCTCA GTGGAACGAA AACTCACGTT AAGGGATTTT GGTCATGAGA 2000
TTATCAAAAAA GGATCTTCAC CTAGATCCTT TTAAATTAAA AATGAAGTT 2050
TAAATCAATC TAAAGTATAAT ATGAGTAAAC TTGGTCTGAC AGTTACCAAT 2100
GCTTAATCAG TGAGGCACCT ATCTCAGCGA TCTGTCTATT TCGTTCATCC 2150
ATAGTTGCCT GACTCCCCGT CGTGTAGATA ACTACGATAC GGGAGGGCTT 2200
ACCATCTGGC CCCAGTGTG CAATGATACC GCGAGACCCA CGCTCACCGG 2250
CTCCAGATTT ATCAGCAATA AACCAAGCCAG CGGGAAAGGGC CGAGCGCAGA 2300
AGTGGTCCCG CAACTTATC CGCCTCCATC CAGTCTATT ATTGTTGCCG 2350
GGAAGCTAGA GTAAGTAGTT CGCCAGTTAA TAGTTGCGC AACGTTGTTG 2400
CCATTGCTGC AGGCATCGTG GTGTCACGCT CGTCGTTGG TATGGCTTC 2450
TTCAGCTCCG GTTCCCAACG ATCAAGGCGA GTTACATGAT CCCCCATGTT 2500
GTGCAAAAAA CGGGTTAGCT CCTTCGGTCC TCCGATCGTT GTCAGAAGTA 2550
AGTTGGCCGC AGTGTATCA CTCATGGTTA TGGCAGCACT GCATAATTCT 2600
CTTACTGTCA TGCCATCCGT AAGATGCTTT TCTGTGACTG GTGAGTACTC 2650
AACCAAGTCA TTCTGAGAAT AGTGTATGCG GCGACCGAGT TGCTCTGCC 2700
CGGCGTCAAC ACGGGATAAT ACCGCGCCAC ATAGCAGAAC TTAAAGTG 2750
CTCATCATTG GAAAACGTTC TTCGGGGCGA AAACTCTCAA GGATCTTACC 2800
GCTGTTGAGA TCCAGTTCGA GTAAACCCAC TCGTGCACCC AACTGATCTT 2850
CAGCATCTT TACTTCACC AGCGTTCTG GGTGAGCAAA AACAGGAAGG 2900
CAAAATGCCG CAAAAAAGGG AATAAGGGCG ACACGAAAT GTTGAATACT 2950
CATACTCTTC CTTTTCAAT ATTATTGAAG CATTATCAG GTTATTGTC 3000
TCATGAGCGG ATACATATT GAATGTATT AGAAAATAA ACAAAATAGGG 3050

B8 cont'd
GTTCCGCGCA CATTCCCCG AAAAGTGCCA CCTGACGTCT AAGAAACCAT 3100
TATTATCATG ACATTAACCT ATAAAAATAG GCGTATCACG AGGCCCTTC 3150
GTCTTCAAG 3159

Please replace the paragraph beginning on page 93, line 1, with the following amended paragraph:

pCK7-96 (Nucleotide residues 3376 to 3881)(SEQ ID NO:39)

B9
AGGAGAATGAATAAATAAAAGTGAATCTTGACCTGTGGTTCTCTCTTCCCTCAATTAAATTATT
ATCTGTTTTACCAACTACTCAATTCTCTTATAAGGGACTAAATATGTAGTCATCCTAAGGCGCATA
ACCATTATAAAATCATCCTCATTCTATTTACCCCTATCATCCTCTGCAAGACAGTCCTCCCTCAA
CCCAACAAGCCTCTGCCTCACAGTCCCCTGGGCCATGGATCCTCACATCCCAATCCGGGGCGCAATT
CGTAATCATGGTCATAGCTGTTCTGTGAAATTGTTATCGCTCACATTCCACACAACATACGAG
CCGGAAGCATAAAAGTAAAGCCTGGGTGCCTAATGAGTGAGCTAACTCACATTAAATTGCGTTGCGCT
CACTGCCGCTTCAGTCGGAAACCTGCGCTGAGCTGCATTAATGAATCGCCAACGCGGGGA
GAGGCGGTTGCGTATTGGCGC

Please replace the paragraph beginning on page 93, line 8, with the following amended paragraph:

B10

pCG7-96 (SEQ ID NO:40)

Please replace the paragraph beginning on page 94, line 12, with the following amended paragraph:

B11

pG4HE (SEQ ID NO:41)

Please replace the paragraph beginning on page 95, line 17, with the following amended paragraph:

B12

10D1 VH(SEQ ID NO:16)

Please replace the paragraph beginning on page 95, line 27, with the following amended paragraph:

B13

10D1 VK(SEQ ID NO:6)

Please replace the paragraph beginning on page 95, line 37, with the following amended paragraph:

B14

4B6 VH(SEQ ID NO:18)